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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/827,484	04/19/2004	Makarand Gore	200315586-1	3315

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HEWLETT PACKARD COMPANY
P O BOX 272400, 3404 E. HARMONY ROAD
INTELLECTUAL PROPERTY ADMINISTRATION
FORT COLLINS, CO 80527-2400

EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
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1612

NOTIFICATION DATE	DELIVERY MODE
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08/14/2008

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

JERRY.SHORMA@HP.COM
mkraft@hp.com
ipa.mail@hp.com

Office Action Summary	Application No. 10/827,484	Applicant(s) GORE, MAKARAND	
	Examiner Gollamudi S. Kishore, Ph.D	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-20, 55, 56 and 60-67 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 17-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-16 and 55-67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment dated 5-9-08 is acknowledged.

Claims included in the prosecution are 1-5, 7-16 and 55-67.

Claim Rejections - 35 USC § 112

1. Claims 1-5, 8-16, 60-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant amends claim 1 to define the vesicles as having an inner membrane and a separate outer membrane and a pharmaceutical payload encapsulate within the inner membrane of each of the said vesicles. A liposome by definition is a bilayer structure and multilamellar liposomes have multiples of bilayers and unilamellar liposomes have a single bilayer, but none of the liposomes have three layers. That is one inner layer surrounded by a bilayer. The lipophilic active agents sequester within the bilayer of the lipophilic phospholipids and hydrophilic active agents sequester within the aqueous interior and the aqueous medium separating the bilayers in a multilamellar liposomes. Lipophilic active agents do not selectively sequester within the inner layer of the bilayer structure. Instant claims 1 and 61-62 exactly indicate such a structure. Instant specification does not teach how to accomplish these structures and how to selectively sequester the active agent in the inner layer of the bilayer structure.

Art Unit: 1612

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 5, 55-56 and 63-67 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear whether the limitation in parenthesis in claim 5 is indeed the limitation.

Applicant's arguments have been fully considered but are not persuasive. Applicant argues that the phrases in parenthesis are part of the claimed subject matter and would be understood by those of ordinary skill in the art. This is not persuasive since it is unclear how one can understand the connection between cholesterol and ovine wool and lipid A and salmonella Minnesota. Applicant has not provided any evidence.

Claim 55 is confusing. It recites, "a **means** for encapsulating said pharmaceutical payload in **a** center of vesicles disposed within". What does the term, 'means' convey in this context? A solvent for the payload? How many centers does the vesicle have?

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-5, 7-8, 10-15, 60 and 61 are rejected under 35 U.S.C. 102(b) as being anticipated by Hsu (5,653,996).

The amended claims require two layers in the vesicles, the inner layer and an outer layer. According to instant claim 1, the active agent is within the inner membrane of each of the vesicles. The term, 'within the inner membrane' can be interpreted in two ways. Since the within the inner membrane is the "aqueous core", the hydrophilic active agent is in the aqueous core or a lipophilic active agent is within the inner membrane itself.

Hsu discloses liposomal formulations containing phosphatidylcholines and phosphatidylglycerol in a buffer solution. The active agents include both water soluble and water insoluble active agents. The compositions further contain a surfactant, Tween which is considered as a solvent besides aqueous medium which is necessary for the formation of a liposome structure (abstract, col. 4, line 52 through col. 6, line 35, col. 9, lines 28-35, examples and claims). The apparatus in Hsu produces both multilamellar and unilamellar liposomes. Although Hsu does not specifically teach the viscosity of the compositions, since instant claims only recite that the viscosity be less than 5 centipoise, it is the examiner's position, in the absence of showing otherwise, that the compositions of Hsu possess the claimed viscosity. The intended use has no significance in composition claims. Since there is aqueous layer between bilayers of multilamellar liposomes, the water soluble active agent would be present in the aqueous layer between the bilayers besides being in the aqueous core of the liposomes meeting the requirements of instant claim 61.

Applicant's arguments have been fully considered, but are not persuasive. As pointed out above, lipophilic (water insoluble) active agents sequester in both layers of the lipophilic phospholipids making up the bilayered liposomes in Hsu. Instant claim language 'comprising' does not exclude the lipophilic active agent sequestering also in the outermost layer of the bilayer. Since Hsu teaches water soluble active agents, they sequester within the aqueous core of the liposomes in Hsu reading on the second interpretation of the claim. The reference still reads on instant claims.

6. Claims 1-5, 7-15 and 60-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Schlossmann (4,976,964).

Schlossmann discloses liposomal dispersions of Nifedipine and dihydropyridines. The phospholipids include phosphatidylcholine and phosphatidylserine. The formulations include glycerol (solvent) and buffers. The sizes of the liposomes are 50-100 nm (Col. 3, lines 20-51 and examples). Although Schlossmann does not specifically teach the viscosity of the compositions, since instant claims only recite that the viscosity be less than 5 centipoise, it is the examiner's position, in the absence of showing otherwise, that the compositions of Schlossmann possess the claimed viscosity. The intended use has no significance in composition claims.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that Schlossmann expressly teaches water-soluble substances are enclosed in the aqueous inner volume of the vesicles rather than a water insoluble payload as claimed. These arguments are not persuasive since as pointed out above instant claims read both ways. Even assuming that instant claims read on water

insoluble payload, Schloomann on column 2, lines 18-22 clearly states "If the compound is lipid-soluble, like dihydropyridine derivatives, it can be incorporated in the lipid membrane, in contrast to water-soluble substances which are enclosed in the aqueous inner volume of the vesicles on (in) the preparation of liposomes".

Furthermore, on col. 1, lines 37-40, Schloomann clearly states that dihydropyridines have poor water solubility. The reference still reads on instant claims.

7. Claims 1-3, 5, 7-8, 12-15 and 60-61 are rejected under 35 U.S.C. 102(b) as being anticipated by Waldrep (5,958,378).

Waldrep discloses liposomal formulations containing cyclosporin. The phospholipids include phosphatidylcholine (abstract, col. 5, lines 25-36, Examples and claims). Although Waldrep does not specifically teach the viscosity of the compositions, since instant claims only recite that the viscosity be less than 5 centipoise, it is the examiner's position, in the absence of showing otherwise, that the compositions of Waldrep possess the claimed viscosity. The intended use has no significance in composition claims.

Applicant provides no specific arguments for this rejection. As pointed out above, instant claims can be interpreted in two ways and the reference of Waldrep still reads on instant claims.

8. Claims 1-5, 7-8, 10-12, 14--15 and 55-56, 63-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallach (5,160,669).

Wallach discloses paucilamellar vesicles containing the insecticide within the central cavity (abstract, col. 1, examples and claims). Wallach discloses further mineral

oil which is a humectant (Table 2). The reference meets the requirements of instant claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hsu or Schlossmann or Waldrep cited above.

The teachings of Hsu, Waldrep and Schlossmann have been discussed above. It is unclear from these references whether the compositions contain claimed amounts of vehicle, vesicle forming component and the payload. Assuming that the amounts are different, it is deemed obvious to one of ordinary skill in the art to use desired amounts of the phospholipids to form required population of liposomes and suspend them in a suitable amount of vehicle. Since the amounts of the active agent depend upon the condition to be treated, this parameter is deemed to be a variable parameter.

Applicant's arguments have been fully considered, but are not persuasive. Applicant's only argument is that to support a rejection of claim, the examiner must begin by identifying whether, how and where each of the limitations of the claim is taught or suggested by the cited prior art. The examiner points out claim 16 merely

Art Unit: 1612

recites the amounts for the components in generic terms and as pointed out above, the examiner has already shown how the prior art meets the requirements of instant claims.

11. Claim 65 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wallach (5,160,669) cited above in view of Handjani (4,608,211).

The teachings of Wallach have been discussed above. What is lacking in Wallach is the inclusion of antifoaming agents, rheology adjusting agent and pH adjusting agents. Such an inclusion however, with a reasonable expectation of success would have been obvious to one of ordinary skill in the art since the reference of Handjani shows the routine practice of adding an antifoaming agent in liposomal compositions (col. 4, lines 1-15).

12. Claims 66-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallach (5,160,669) cited above in view of Schlossmann (4,976,964).

The teachings of Wallach have been discussed above. What is lacking in Wallach is the inclusion of rheology adjusting agent and pH adjusting agents. Such an inclusion however, with a reasonable expectation of success would have been obvious to one of ordinary skill in the art since the reference of Handjani shows the routine practice of adding buffers and glycerol in liposomal compositions (col. 3, line 27 through col. 4, line 66).

US 2008/0070944 which states that mineral oil is a humectant and Milne (5,958,463) which shows the common practice of the addition of antifoaming agent are cited of interest (0186).

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1612

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

GSK